UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

August 12, 1993

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

EPA-SAB-DWC-93-016

Honorable Carol M. Browner
Administrator
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Subject: SAB Review of the ongoing revision of the methodology for deriving National Ambient Water Quality Criteria for the protection of human health.

Dear Ms. Browner:

The Clean Water Act of 1977 required EPA to develop Ambient Water Quality Criteria (AWQC) for ambient water contaminants that may adversely affect human health. In 1980, the Agency published the methodology for the development of AWQC and summaries of the criteria for 65 chemicals and chemical classes. There have been many scientific advances relevant to AWQC since that time, however, and the Office of Water (OW) is now revising the methodology. On February 9-10, 1993, the Drinking Water Committee of the Science Advisory Board (SAB) met to review the ongoing revision of the 1980 methodology for deriving National Ambient Water Quality Criteria (AWQC). The charge to the Committee focused on the human health aspects of the AWQC and outlined critical issues in six subject areas, namely Cancer Effects, Non-Cancer Effects, Bioaccumulation, Exposure, Microbiology, and Minimum Data Requirements.

The Committee was pleased to learn of this important activity. The Office of Water is clearly engaged in a systematic effort to develop a state-of-the-science approach to revising the 1980 methodology. The process followed by the OW to identify the weaknesses in the methodology included the development and wide circulation for comment of issue papers, followed by a workshop of experts which produced the basis for the document reviewed by the Committee. We believe that this process was well thought-out and helped to

clearly define many of the critical scientific issues and options concerning the methodology.

The Committee is concerned, however, that some of the approaches being considered for setting AWQC by the Agency do not reflect the necessary strategy of emphasizing regulation of contaminants in the medium (or media) where each contaminant is most likely to cause adverse effects. Instead, the Agency approach focuses almost exclusively on point source discharges to water and fails to place the exposures resulting from them in proper perspective. We are concerned that setting AWQC in this manner could result in the expenditure of large sums of money without achieving significant reductions in human exposure and risks.

The Committee also wishes to emphasize that we foresee considerable difficulty in using the concept of Maximum Contaminant Level Goals (MCLGs) in the development of AWQC methodology. Introducing this concept into the AWQC is likely to confuse the public, distort the relative importance of carcinogens (versus untested contaminants), incorrectly mix carcinogenic and non-carcinogenic effects in an unscientific manner, and result in the misdirection of resources if applied to the permitting process.

In the remainder of this letter we summarize the major findings of the review in each of six subject areas that encompassed the charge to the Committee. The accompanying report discusses these issues more fully.

Cancer Effects

Because carcinogenic risk assessment has evolved substantially since 1986, we do not favor the interim adoption of the 1986 Cancer Risk Guidelines for the revised AWQC methodology. Instead, the Committee urges the Agency to expedite the revision and publication of updated guidelines, and to seek SAB review of that revision.

We urge the Agency to develop and use more accurate indications of the uncertainty of cancer risk estimates than the currently-used upper and lower confidence intervals of the linearized multi-stage model (LMS). The Committee also suggests that the Agency routinely provide risk managers with *examples* of comparable past estimates of cancer risk and their corresponding administrative outcomes, to help ensure that decisions are made with knowledge and

appreciation of past Agency experience, while also making sure to incorporate advances in scientific knowledge.

Finally, the Committee recommends that the Agency tackle decisions on Group C chemicals on a case-by-case basis, based on a clearly-defined process that adequately defines the weight that will be given to different types of evidence.

Non-Cancer Effects

We agree with the Agency that the severity of effects should be considered in the development of a Reference Dose (RfD), but we find the scale(s) that is being applied by the Agency to this problem inadequate. We urge the Agency to consider the alternative approach discussed in our report.

The Committee believes that the precision of a given RfD must be based on specific data sets for specific RfDs, and suggests that the Agency consider reporting the range from a calculated RfD to the lowest observed adverse effect level as a useful measure of such precision.

The Committee generally endorses the use of the benchmark dose by the Agency and supports the use of PB-PK models (physiologically-based pharmokinetic models) for RfD determination. However, we warn against the dangers of using the results of short-term tests to establish anything other than interim RfDs.

Bioaccumulation and Exposure Issues

We strongly urge the Agency to base AWQC on sound experimental evidence that bioaccumulation *does* occur, rather than on hypothetical assumptions that bioaccumulation *might* occur. The Committee believes that the strategy of setting AWQC by measuring contaminant concentrations in certain biota and then applying either a bioconcentration factor (BCF) or a bioaccumulation factor (BAF) to calculate water concentrations may not accurately reflect the complex ways in which the real environment operates. Although we support the Agency's efforts to develop well-validated BAFs, for the time being we recommend that the Agency rely more heavily on BCF rather than BAF, because of the higher likelihood of collecting an adequate BCF database,

The Committee does not feel that it is appropriate to develop AWQC geared to ensure that the sum of all theoretically possible exposures *never* exceeds the RfD by even a small amount. We reject the routine use of the percentage or subtraction methods for the allocation of the RfD, and the use of default values, in the absence of reliable exposure data. Instead, we endorse the recommendation from the AWQC workshop held by the Agency in 1992 which calls for bringing together all the appropriate offices or agencies when significant contributions to exposure are expected from multiple sources, and the total of those contributions exceeds the RfD.

Finally, the Committee feels that the best way to protect subpopulations with high fish consumption is to base health standards on the levels of chemical which are found in fish, not in effluents.

Microbiology Issues

The Committee found that the Agency was attempting to simultaneously tackle too many issues related to the regulation of microbiological contaminants. We strongly urge the Agency to set priorities and to focus efforts on ambient recreational waters, which are not covered by other regulations or agencies. We also recommend the formation of a multi-institutional workgroup to help EPA and other agencies (e.g., Centers for Disease Control and Prevention, Food and Drug Administration) address scientific and technical issues concerning microbiological contaminants in ambient waters in a holistic manner.

The Committee generally favors a risk-based approach to criteria for pathogenic organisms in ambient waters. We are also aware that there are major gaps in epidemiologic research in microbiology and thus recommend the coordination of research and risk assessments for pathogenic microbes in ambient waters with assessments being done for other waters. The Committee supports an approach based on the likelihood of human exposure to different types of ambient water as the basis for identifying the types of waters for which criteria need to be developed. We believe that AWQC for microbes should include fecally-transmitted diseases other than gastroenteritis, as well as microbes causing diseases of organs other than the GI tract.

The Committee also commented on the appropriateness of the currently-approved indicator organisms for determining the safety of bathing waters, as

well as on research needs and their priority in the context of the ambient water quality criteria initiative.

Minimum Data Requirement Issues

The Committee generally found the tiered approach presented by the Agency to categorize the availability of data to be reasonable. We have serious concerns regarding the classification of chemicals in categories (e.g., Group C) where they may not properly belong, so that a regulatory decision can be made, or the use by the states of Tier III values to set permanent permit levels. Finally, the Committee recommended certain criteria that might be applicable to the proper use of 28-day study data in developing interim toxicity values.

Additional detail on the above issues can be found in the complete report by the Committee, which is attached. We should also stress that we did not attempt to comprehensively review all the issues discussed in this report. We look forward to revisiting many of these critical issues with your staff in the future, as they continue to revise the 1980 AWQC methodology. The Committee appreciates the opportunity to conduct this review, and we look forward to your response to the scientific advice transmitted herein.

Sincerely,

Raymond C. Loehr

Dr. Raymond C. Loehr, Chair
Executive Committee
Science Advisory Board

Verne A. Ray

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Science Advisory Board

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EPA

REVIEW OF THE METHODOLOGY FOR DEVELOPING AMBIENT WATER QUALITY CRITERIA FOR THE PROTECTION OF HUMAN HEALTH

PREPARED BY THE DRINKING WATER COMMITTEE OF THE SCIENCE ADVISORY BOARD

NOTICE

This report has been written as a part of the activities of the Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report do not necessarily represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use.

ABSTRACT

On February 9-10, 1993, the Drinking Water Committee of the Science Advisory Board (SAB) reviewed the Agency's revision of the methodology for deriving National Ambient Water Quality Criteria (AWQC) for the protection of human health.

The Committee was pleased to learn of the Agency's systematic effort to revise this methodology. They were critical of the emphasis given to point source discharges in the ongoing revision. They commented on the Agency's revision of its 1986 Cancer Risk Guidelines, on the need to incorporate mechanistic information in them, and on the Agency's treatment of Group C chemicals and uncertainty. They addressed issues of severity scales for non-cancer effects, the development and allocation of RfD values, the use of short-term study data, Health Advisory Doses, and the benchmark dose. They reviewed the Agency's use of Bioaccumulation Factors (BAFs) and Bioconcentration Factors (BCFs), the use of MCLGs (Maximum Contaminant Level Goals) in AWQC methods, and the use of separate criteria for drinking water and fish intake.

The Committee urged EPA to priority-rank the needs related to microbiologic exposures in and supported the use of new structures to assist EPA. They recommended exposure potential as the basis for microbiological criteria, and supported a risk-based approach to the regulation of microbes. They commented on the relationship of indicator organisms to non-GI illnesses, the efficacy of indicators in tropical waters, and research needs on determinants of virulence, injured pathogens, and molecular techniques for pathogen identification.

The Committee also reviewed the proposed use of a tiered approach to categorize data availability, and addressed issues concerning the categorization of Group C chemicals under this scheme.

Key Words: Cancer, Risk Assessment, RfD, Ambient Water Quality Criteria, Non-Cancer Risk, Bioaccumulation, Exposure, Minimum Data Requirements, Point Source Discharges, Microbiological Contaminants, Group C Chemicals, Bioconcentration.

ENVIRONMENTAL PROTECTION AGENCY
SCIENCE ADVISORY BOARD
DRINKING WATER COMMITTEE

Review of Revision of Methodology for Ambient Water Quality Criteria

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1. EXECUTIVE SUMMARY

On February 9-10, 1993, the Drinking Water Committee ("the Committee") of the Science Advisory Board met to review the Agency's ongoing revision of the methodology for deriving National Ambient Water Quality Criteria (AWQC) for the protection of human health. A document summarizing the revision process, prepared by the Human Risk Assessment Branch (HRAB) of the Office of Water (OW) was presented and discussed ("Revision of Methodology for Deriving National Ambient Water Quality Criteria for the Protection of Human Health: Report of Workshop and EPA's Preliminary Recommendations for Revision"). The Committee was pleased to learn that the Agency is engaged in a systematic effort to develop a state-of-the-science approach to revising the 1980 methodology. The review focused on key questions posed to the Committee in six subject areas: Cancer Risk, Non-Cancer Risk, Bioaccumulation, Exposure, Microbiology, and Minimum Data Requirements.

1.1 Cancer Risk Issues

a) The Committee was pleased to learn that the Agency's 1986 Cancer Risk Guidelines are beginning to undergo revision and urged the Agency to incorporate in the revised Guidelines, as well as in the AWQC methodology, the growing body of scientific knowledge regarding carcinogenic mechanisms that has accumulated since the Guidelines were adopted. Because carcinogenic risk assessment has evolved substantially since 1986, the Committee rejected the interim adoption of the 1986 Guidelines in AWQC methodology, and instead urged the Agency to expedite the review and publication of updated Guidelines. The Committee also recommended that any new Guidelines be appropriately reviewed by a multidisciplinary SAB commmittee.

b) With regard to the characterization of risk, the Committee suggested that the Agency routinely provide risk managers with risk estimates that are placed in appropriate context with *examples* of comparable past estimates of risk and their corresponding

administrative outcomes. This approach would help ensure that decisions are made with knowledge and appreciation of past Agency practices, while also making sure to incorporate advances in scientific knowledge.

c) The Committee rejected the current approach of using the upper and lower confidence intervals of the linearized multi-stage model (LMS) as a meaningful estimate of the uncertainty around the point estimate of risk, because these intervals are only a measure of the uncertainty of a non-verifiable model, and do not convey the uncertainty of interspecies or low-dose extrapolations. Instead, the Committee suggested that the Agency develop more meaningful indications of the uncertainty of risk estimates.

d) Finally, the Committee recommended that the Agency tackle decisions on Group C chemicals on a case-by-case basis, based on a clearly-defined process that adequately defines the weight that will be given to different types of evidence.

1.2 Non-Cancer Risk Issues

a) The Committee agreed with the Agency that the severity of effect should be considered in the development of a Reference Dose (RfD), but considered that the scale(s) that are being applied by the Agency to this problem are vague and prior pronouncements and studies conducted in various offices within the Agency have confused rather than clarified the issue. Of three scales that may be applicable, the Committee considered that the one with the widest applicability for non-cancer risks would be a scale based on whether the effect represents actual pathology (e.g. extensive necrosis), a functional deficit (e.g., paralysis, learning deficits, impaired biliary secretion), a biochemical change that is clearly related to an adverse effect, or simply a biochemical or behavioral change of unknown consequence.

b) The Committee believes that defensible statements about the precision of a given RfD must be based on specific data sets for specific RfDs, and that reporting the range from a calculated RfD to the lowest observed adverse effect level may serve as one useful

measure of precision of an RfD, because it would essentially define the uncertainty of an estimated "safe" exposure level.

c) The Committee believes that PB-PK modeling can be useful for RfD determination. This utility is greatly enhanced when there is reasonably good understanding of the mechanisms by which the chemical is acting.

d) The Committee concluded that important toxic effects could be missed because of the possibility of false negative findings arising from studies of less than 90 days exposure. To guard against this danger, they recommend that data from such tests only be used to set interim or temporary RfDs.

e) The Committee rejected the use of site-specific Health Advisory Doses (HADs) for one-day and even longer term exposures in the context of ambient water quality.

f) The Committee generally endorsed the use of the benchmark dose by the Agency, but emphasized several potential pitfalls of this method.

1.3 Bioccumulation and Exposure Issues

a) The Committee cautions the Agency that the strategy of setting AWQC by measuring contaminant concentrations in certain biota and then applying either a bioconcentration factor (BCF) or a bioaccumulation factor (BAF) to calculate water concentrations may not accurately reflect the complex ways in which the real environment operates. The report describes a number of instances where problems may arise with this approach and urges the Agency to base AWQC on sound experimental evidence that bioaccumulation *does* occur, rather than on hypothetical assumptions that bioaccumulation *might* occur. The Committee recommended that, for the time being, the Agency focus attention on BCF rather than BAF, because of the higher likelihood of collecting an adequate BCF database.

b) With regard to allocation of the RfD, the Committee did not feel that it is appropriate to develop AWQC geared to ensure that the sum of all theoretically possible exposures never exceeds the RfD by even a small amount. They rejected the routine use of the percentage or subtraction methods, and the use of default values in the absence of reliable exposure data. Instead, the Committee endorsed the recommendation from the AWQC workshop held by the Agency in 1992 which calls for bringing together all the appropriate offices or agencies when significant contributions to exposure are expected from multiple sources, and the total of those contributions exceeds the RfD. Finally, the report recommended the use of separate criteria based on fish intake and water consumption (i.e., hypothetically using up all the RfD in each calculation).

c) The Committee foresees considerable difficulty in using the concept of Maximum Contaminant Level Goals (MCLGs) in the development of AWQC. Introducing this concept into the AWQC is likely to confuse the public, distort the relative importance of carcinogens (versus untested contaminants), incorrectly mix carcinogenic and non-carcinogenic effects in a non-scientific manner, and result in the misdirection of resources if applied to the permitting process.

d) The Committee noted that current "average fish consumption" rates of 6.5 g/day may not be protective for potential acute effects associated with a large single meal of fish, and believes that criteria for acute effects may need to be developed when it can be reasonably anticipated that single exposures may induce adverse effects in humans.

e) The Committee feels that circumstances in which a separate criterion for incidental ingestion would be necessary are so rare that they do not warrant serious consideration by the Agency (i.e., situations where drinking water criteria are not used, such as estuaries, and fish ingestion or aquatic life criteria do not protect recreational users from incidental ingestion).

f) The Committee feels that the best way to protect subpopulations with high fish consumption is to base health standards on the levels of chemical which are found in fish, not in effluents.

1.4 Microbiology Issues

a) The Committee found that the Agency was attempting to tackle too many issues related to the regulation of microbiological contaminants at the same time, with insufficient resources. They strongly urged the Agency to set priorities and to focus its efforts on ambient recreational waters, which are not covered by other regulations or agencies, and to leave other waters (e.g., drinking source waters, shellfishing waters) to be addressed through existing regulatory programs. The Committee also supported the formation of a multi-organizational workgroup to help EPA and other agencies (e.g., Centers for Disease Control and Prevention, Food and Drug Administration) address scientific and technical issues concerning microbiological contaminants in ambient waters in a holistic manner.

b) The Committee generally favored a risk-based approach to criteria for pathogenic organisms in ambient waters, but they were also aware that there are major gaps in epidemiologic research in microbiology that must be addressed, and they recommended the coordination of research and risk assessments for pathogenic microbes in ambient waters with assessments being done for other waters. The Committee also supported an approach based on the likelihood of human exposure to different types of ambient water as the basis for identifying the types of waters for which criteria need to be developed, and the inclusion of microbes causing fecally-transmitted diseases other than gastroenteritis, as well as microbes causing diseases of organs other than the GI tract. Finally, they do not believe that current ambient *recreational* water quality criteria are appropriate or transferable to *other* ambient waters.

c) The Committee believes that the currently-approved indicator organisms in beach waters are not always appropriate for determining the safety of bathing waters with respect to gastro-intestinal (GI) disease, that these organisms are not likely to be

adequately predictive of the human health risks from non-GI illnesses associated with human or animal fecal contamination, and that their validity and usefulness in tropical ambient waters is uncertain. They are also of the opinion that there are candidate alternative indicators worthy of consideration and deserving of investigation in this initiative, including several examples mentioned in the workshop report and EPA's response.

d) Finally, the Committee believes that research efforts in other areas, including the virulence determinants of microbial pathogens, the public health significance of injured pathogens, and current molecular techniques for pathogen detection and identification are important but are beyond the scope of the ambient water quality criteria initiative and should be of low priority in this regulatory context.

1.5 Minimum Data Requirement Issues

a) The Committee generally found the tiered approach presented by the Agency to categorize the availability of data to be reasonable. The report addresses certain aspects of the criteria for each tier in the proposed system.

b) With regard to the categorization of Group C chemicals, the Committee feels that it would be inappropriate to place a chemical in a category where it does not belong so that a regulatory decision can be made, and that allowing the states to use Tier III values to set permanent permit levels would be very risky.

c) The Committee discussed certain criteria which might be applicable to the proper use of 28-day study data in developing interim toxicity values.

2. INTRODUCTION

2.1 Background

The Clean Water Act of 1977 (Public Law 95-217) required EPA to develop Ambient Water Quality Criteria (AWQC) for ambient water contaminants that may adversely affect human health. In 1980, the Agency published the methodology for the development of AWQC in the Federal Register (US EPA, 1980). They also published summaries of the criteria for 65 chemicals and chemical classes and announced their availability to the public. The criteria contain recommended maximum permissible pollutant concentrations consistent with the protection of human health, aquatic organisms, and some recreational activities.

There have been many advances in scientific disciplines relevant to the evaluation of ambient water quality and the development of criteria since 1980, and hence the Human Risk Assessment Branch (HRAB) of the Office of Water (OW) is now undertaking a large scale review and revision of the 1980 criteria methodology. As part of the revision process, the HRAB/OW organized a workshop of experts in September of 1992 to examine a set of critical issues concerning the methodology. The workshop participants were organized into six subject areas, depending on their expertise. The six areas were Cancer Risk, Non-Cancer Risk, Bioaccumulation, Exposure, Microbiology, and Minimum Data Requirements. Each work group reviewed a set of detailed issue questions and developed relevant recommendations.

Based on the outcome of the Workshop, the HRAB/OW prepared a draft report entitled "Revision of Methodology for Deriving National Ambient Water Quality Criteria for the Protection of Human Health: Report of Workshop and EPA's Preliminary Recommendations for Revision" (henceforth the "Report"). This draft report defined critical issues in each of the six subject areas listed above, summarized the recommendations arising from these areas in the Workshop (including minority opinions), and reported the Agency's (HRAB/OW) own preliminary recommendations in each area.

2.2 Charge To The Committee

In its original charge, the HRAB/OW requested that the Drinking Water Committee ("the Committee") of the Science Advisory Board (SAB) review the general direction of the revision process underway for the criteria methodology. Specifically, the charge was to (a) review each of the critical issues addressed by subject areas, and (b) review the workshop recommendations and the preliminary HRAB/OW recommendations summarized in the Report.

Based on the discussions during the meeting of February 9-10, 1993, the HRAB/OW modified the charge to the Committee. The new charge had the same broad objectives, but addressed a somewhat reduced number of priority questions concerning each of the six areas into which the document is organized. The Committee findings are reported in Chapter Three of this report, which is organized into the six subject areas described above. Because of the wide range of issues tackled by this review, the Committee did not attempt to treat them all comprehensively. Indeed, the Committee expects to revisit a number of these issues in more depth in future reviews.

3. FINDINGS

3.1 Introduction

The findings in this Chapter are organized following the six subject areas described earlier, namely Cancer Risk, Non-Cancer Risk, Bioaccumulation, Exposure, Microbiology, and Minimum Data Requirements. Before describing the specific findings in this manner, however, the Committee wishes to address several key general issues concerning AWQC.

The Committee was pleased to learn of this important activity. The Office of Water is clearly engaged in a systematic effort to develop a state-of-the-science approach to revising the 1980 methodology. The process followed by the Office to identify the weaknesses in the methodology included the development and wide circulation for comment of issue papers, followed by a workshop of experts which produced the basis for the document reviewed by the Committee. We believe that this process was well thought-out and helped to clearly define many of the critical scientific issues and options concerning the methodology.

The Committee is of the opinion, however, that the Agency should make a determined effort to begin regulation of contaminants in the medium (or media) where the contaminant is most likely to cause adverse effects. This means that some contaminants would best be regulated by setting standards based on fish consumption, and others by developing standards based on water, air, air plus water, etc. Such an effort requires special coordination among the various regulations for which EPA is responsible as well as some regulations for which EPA is not responsible. In her recent interview in Chemical & Engineering News Administrator Browner addressed concerns of this type when she said that "the goal of an agency like EPA should be to look across [these various laws] to see how they can be integrated into a more meaningful regulatory scheme, an environmental protection plan (C&E News, 1993)." She went on to indicate that such integration must cut across Agency boundaries.

The Committee feels that some of the approaches being considered for setting Ambient Water Quality Criteria (AWQC) by the Agency do not reflect this important and appropriate strategy. The document provided by the Agency for review focuses almost exclusively on point source discharges to water and

fails to place the exposures resulting from them in proper perspective. The Committee is concerned that setting AWQC in this manner could result in the expenditure of large sums of money without achieving significant reductions in human exposure and risks.

Because aquatic systems often receive contaminants from multiple point and non-point sources (including fallout from the air), the concentration of a given chemical in ambient water may exceed proposed criteria even before the contribution from any single point source is added. Thus a point source might find itself in the position of being legally unable to discharge water of the same quality it obtained from ambient water, even if it did not itself contribute to the presence of those contaminants. For example, a situation could occur in which a wastewater treatment plant receiving chloroform from drinking water disinfection at a level of 50 μg/l may not be able to discharge this water without violating AWQC.

3.2 Cancer Risk Issues

The Committee was asked to comment on a number of critical scientific issues concerning the assessment of carcinogenic risk during its review of the methodology for developing ambient water quality criteria (AWQC). Many of these issues are also currently being examined by the Agency as part of its revision of the 1986 "Guidelines for Cancer Risk," although this process is still at a very early stage, judging from the briefing provided to the Committee. The overlap of these two revision processes in the Agency requires that the Committee place its comments on specific cancer risk assessment issues for the AWQC methodology in the proper context.

The Committee believes that the update of the 1986 Guidelines is among the most important activities within the Agency at this time. There have been substantial advances in our understanding of cancer in the past few years, including important insights into mechanisms of carcinogenesis, and the Agency should seek to incorporate these advances into the revised Guidelines. Moreover, it is unlikely that the Agency will be able to deal effectively and consistently with problems in other water programs, such as disinfection by-products, without updating the Guidelines.

Before new Guidelines are adopted, however, the Committee feels that they should be reviewed by the SAB, perhaps utilizing a special *ad hoc*

committee constituted from members from several committees. This is critical because the guidelines impact the work of many EPA program offices and thus the expertise and concerns of many committees. Also, the guidelines should be revised in such as way that they can be applied consistently across EPA.

It is also critical that the Agency clearly define the objectives of the revision, and the Committee feels that one such objective must be to develop a more scientifically-based rationale for classification of chemicals, with greater weight given to mechanistic data than is the case today. The Agency should make sure that the new guidelines improve regulatory policy and practice, and that they will facilitate the management of difficult cases, rather than maintaining the regulatory boundaries that are in the present scheme. A serious concern to the Committee is whether revised Guidelines would permit new concepts and data to be incorporated quickly, as they are validated in the scientific world, or whether each new scientific development would need to be officially recognized through a lengthy process before it can be adopted by the Agency's guidelines.

These and other critical questions should be part of the EPA's revision of the 1986 Guidelines. Until that revision is complete and a more comprehensive draft of the revised Guidelines is available, however, our comments in the area of cancer risk assessment for AWQC must be viewed as preliminary. They will need to be re-examined in context when the revision of the Guidelines is closer to completion.

a) **Should the 1986 EPA Cancer Assessment Guidelines be adopted with allowance for flexibility as the new revised Guidelines are published? Should emphasis be placed on mechanistic data and route and level of exposure to assist in interpretation of relevance of tumor occurrence, as discussed in the draft revised Cancer Guidelines?**

The 1986 EPA Cancer Guidelines should not be adopted for the revised AWQC methodology. There has been substantial progress in our understanding of cancer since 1986. The "Working Paper" for the new guidelines includes consideration of many advances in cancer research during this period whose implementation would significantly affect risk assessments outcomes. For the Agency to continue to rely on the old Guidelines in the development of water

quality criteria has the potential of creating considerable confusion in the future.

It is laudable that the EPA "Guidelines for Cancer Risk" should be reexamined in light of changes in our knowledge. Clearly, we are beginning to glimpse the broad mechanistic landmarks of carcinogenesis for some cell and tumor types. We can begin to understand some cases of genetic predisposition to cancer and have identified a number of oncogenes and tumor suppressor genes which appear to regulate cell growth and differentiation. Because more comprehensive mechanistic insights are likely to emerge in the future, we need to have the flexibility of mind and regulatory process to respond to these advances as they occur. For example, mechanistic insights should allow better understanding of which experimental findings may not be applicable to humans (e.g., alpha-2μ-globulin production and susceptibility to the carcinogenicity of gasoline in male rat kidneys). New methods are allowing us to identify the biological consequences of exposures as genetic alterations, and to measure the doses to genes that are important to cancer induction. We have increasing knowledge about the kinds of lesions that particular carcinogens produce and the spectrum of sites they affect in particular genes. We even have growing insight about spontaneous genetic events, some of which may represent oxidative damage to genes and/or chromosomes in addition to replication errors. The insights that these advances may bring to the risk estimation process should not be ignored.

Data on genetic activity of chemicals in short and long term tests *in vitro* and even *in vivo* should be given greater weight in the future. However, the incorporation of this information in risk assessment *should emphasize the relationships between specific mutation sites, the resulting alterations in specific proteins, and the development of cancer.* The simple identification of the ability of a given compound to produce mutations in various test systems has limited utility in risk assessment, beyond the ability of classifying compounds as putative mutagens or non-mutagens. Studies that give insight into the normal and abnormal behavior of human cells and tissues should be used to help bridge the gap between studies in animals and effects in human beings. Powerful new methods to assess environmental exposures to chemicals and internal doses should be employed where possible to build the data bases needed to link dose and effect more precisely.

The use of genetic toxicology for classifying the mutagenic potential of chemicals needs to be more critically evaluated than in the past, particularly with reference to the magnitude of doses that are required to produce effects. This is a particularly important issue in the interpretation of data from chemicals that give rise to clastogenic effects in the absence of an ability to induce point mutation.

b) Should risk be presented in two ways? (1) Point estimate with indication of uncertainty; (2) Set of credible alternative estimates based on applicable models.

Estimates of risk are intended to be used as input information by risk managers. The estimates of risk are usually derived from a limited body of data, numerous extrapolations are necessary, and the resulting risk estimate is typically limited by the intrinsic error in the data and propagation of these errors through the extrapolation processes. The methods used for extrapolation or the concepts upon which they are based may, with the advance of scientific knowledge, be proven incorrect. The Committee therefore recommends that risk estimates be presented in both manners: (1) as point estimates of risk with an indication of the uncertainty of the estimate, *and* (2) as a collection of credible alternate estimates based on *applicable* models (i.e., mechanistic models, not alternative statistical models which cannot be experimentally verified in any practical manner).

Moreover, because it recognizes that risk estimates are likely to be imprecise, the Committee feels that it is important to provide risk managers with risk estimates that are placed in appropriate context. The Committee suggests that the Agency routinely provide assessments to risk managers with *examples* of comparable past estimates of risk and their corresponding administrative outcomes. This approach would help ensure that decisions are made with knowledge and appreciation of past Agency practices, while also making sure to incorporate advances in scientific knowledge. It would permit the Agency to know, for roughly comparable situations, that risk estimates and administrative decisions do not differ (weighing costs against risks) by more than an order of magnitude, without an explicit decision to that effect. Such examples of past practice should not seek to "freeze" the Agency's science, but rather to ensure that estimates take into account *both* past Agency practice and the evolution of scientific knowledge.

The Agency must also be very careful how it expresses uncertainty. The conventional use of the upper 95% confidence limit of the LMS (linearized multi-stage model) estimate of risk has introduced a great deal of confusion into the analysis of uncertainty. The LMS convention was adopted primarily because it yields a more stable estimate of risk than the maximum likelihood estimate (i.e. the Maximum Likelihood Estimate or MLE is too sensitive to the data). Therefore, the difference between the MLE and upper 95% confidence limit is more of a measurement of how poorly the data fit the upper 95% confidence limit of the extrapolation from the model than any real expression of uncertainty. The Committee rejects the current approach of using the upper and lower confidence intervals of the LMS as a meaningful estimate of the uncertainty around the point estimate of risk, because it is an extrapolation beyond available data or experimental confirmation. The point estimates currently in use by the Agency *almost always* involve extrapolations over orders of magnitude, based on assumptions that may be incorrect in many cases. To employ such figures as meaningful estimates of the uncertainty in the results of a risk assessment is clearly not appropriate. A more accurate indication of the uncertainty would be simply to state the extent to which these estimates are extrapolations (e.g., compare the lowest dose that has been shown to produce cancer in a valid study to the model estimate in the same units).

c) **Should decisions on Group C Chemicals (whether to use the RfD approach or cancer quantification by LMS) be made on a case-by-case basis after consideration of the appropriate level of concern and appropriateness of the data?**

We recommend that the Agency address these situations on a case-by-case basis, based on a clearly-defined process, particularly with respect to the weight that will be given to different types of evidence.

The Group C category is a reflection of the 1986 Guidelines. As stated in item a above, the Committee strongly supports the revision of those Guidelines to include mechanistic information and perhaps, as was suggested during the briefings, elimination of the weight of evidence categorization of carcinogens. In this context, the comments that follow may soon become outdated by revised Guidelines.

Group C chemicals are a very heterogeneous collection. At one extreme, some chemicals are in this class because there is a tenuous indication of

carcinogenicity from isolated evidence of an increase in rates of cancer in one species or sex, in one organ (often with tumors that commonly occur spontaneously in that organ), or even because of a structural similarity to an established carcinogen. *This results in the placement of chemicals into this category even when they have been adequately studied and found negative in several other animal species (e.g., tetrachloroethylene, trichloroethylene, numerous pesticides).* Such chemicals also lack human carcinogenesis data, since positive human findings would have resulted in a higher ranking of the chemical. *Such chemicals frequently may be best treated by the RfD approach.* At the other extreme, there are chemicals that would have been classified in class B if only some of the available data were slightly stronger (e.g., with good dose response information). *In such instances where scientific judgement would suggest that the lower classification is simply the result of limited data, prudence may dictate the additional conservatism of the linearized multistage model.*

Given such diversity in the chemicals currently in Group C, there is room to make distinctions between those posing likely carcinogenic risk and those with little probability of carcinogenicity. At the extremes discussed above, it would be appropriate to treat chemicals with the highest probability of risk of carcinogenicity as if they were carcinogens, while the chemicals least likely to be carcinogens are treated with the RfD approach and appropriately conservative uncertainty factors, as described above.

The problematic chemicals, however, will be those that fall between these extremes. Should they be assessed as carcinogens or not? *In these cases, it may be appropriate to rely on ancillary data to provide insight into the mechanism by which the chemical is acting. For example, is there evidence that the chemical is mutagenic with appropriate consideration of the doses used in the test systems? What other types of effects does it have in the target organ that may be influencing the development of cancer? Is the chemical related to other chemicals that are recognized chemical carcinogens?*

3.3 Non-Cancer Risk Issues

a) **Should the methodology (following the EPA noncancer health effects guidelines) expand on the aspects of severity of effect and presentation of the RfD?**

There is no question that the severity of effect should be considered in the development of a RfD. However, the scale(s) that are being applied by the Agency to this problem are vague and prior pronouncements and studies conducted in various offices within the Agency have confused rather than clarified the issue. Theoretically, scales of severity could be constructed based on: (1) whether the effect is reversible, or irreversible and cumulative; (2) whether the effect represents actual pathology (e.g. extensive necrosis), a functional deficit (e.g., paralysis, learning deficits, impaired biliary secretion), a biochemical change that is clearly related to an adverse effect, or simply a biochemical or behavioral change of unknown consequence; or (3) simply by the target organ affected.

These potential severity scales would have different applications. Clearly, the first is easily related to assumptions about chemical carcinogenesis, but also selectively applies to some neurotoxic and reproductive effects (e.g., effects of acrylamide or n-hexane) and perhaps other effects.

For most non-cancer risks, however, the second scale will probably have the greatest applicability. Serious consideration should be given to determining how dose-response relationships for an effect measured at the biochemical level are related to modifications in function and to the development of overt pathology in several target organs. In the meantime, it is very important that the categorization of these effects continue to be emphasized in the development of a RfD, particularly when it is developed from a LOAEL. These considerations should also be made explicit when developing an RfD from a NOAEL, reducing the standard uncertainty factors when the NOAEL is based on biochemical effects at exposures below those which produce overt toxic effects.

The third option requires that different values be given to different organs or systems, something that is not easily dealt with beyond a few trivial examples. Consequently, the Committee is skeptical about the value of such a scale.

b) **Should an RfD range estimate be presented, considering that currently the RfD is an estimate with a precision varying within an order of magnitude?**

The notion that the RfD is roughly accurate within an order of magnitude seems to imply that there is some way to evaluate the precision of a particular RfD. There is little data of which the Committee is aware that would actually support the application of the term precision to this effort. More defensible statements about the precision of any given RfD would have to be based on specific data sets for specific RfDs. The range from the calculated RfD to the lowest observed effect level may serve as one useful measure of precision of an RfD, because it would essentially define the uncertainty of an estimated "safe" exposure level. It would be very important that the seriousness of the effect observed at the LOAEL be made clear if such an approach is utilized.

c) Should PB-PK and dosimetry modeling be used for RfD determination?

The Committee believes that PB-PK modeling can be useful for RfD determination. This utility is greatly enhanced when there is reasonably good understanding of the mechanism by which the chemical is acting.

d) Should studies of less than 90 days exposure (e.g., 28-30 days) be used with uncertainty factors for RfD determination?

No justification was provided for the use of data from a 28-30 day exposure for estimating an RfD. Moreover, there is no real definition of what would be examined in a 28-30 day experiment. In some cases such data might be utilized. For example, if such an experiment were to include a genuine attempt to identify target organs by doing comprehensive histopathological examination of organs, the results might be used on a temporary basis. This could be particularly important if the results provided clear indications of adverse effects. However, the use of *negative* data from such short term experiments would miss effects that take longer periods of time to develop, and thus could be quite dangerous. Finally, there are experiments of this length that are performed for reasons other than safety evaluation (e.g., focusing on whether a particular biochemical effect occurs or not) which may be important in providing mechanistic data to explain results in other studies. However, this type of data should not be used as the sole basis for developing an RfD, unless the pharmacodynamic relations between the biochemical interactions and the toxicologic response is understood in quantitative terms.

The danger of false negative findings from short-term studies, both 30- and 90-day, also exists for non-cancer effects that simply will not be apparent in such studies, including reproductive effects, teratogenesis and developmental toxicities. Consequently, RfDs based on such data must clearly be labeled as being *interim or temporary*. The establishment of such RfDs should consider the additional uncertainty created by the fact that such effects have not be evaluated.

e) **Should site-specific health advisory doses (HADs) for one day and longer-term exposure situations be derived, rather than ambient water criteria based on life-time exposure?**

The application of a site-specific Health Advisory Doses (HADs) in the context of ambient water quality criteria is of questionable utility. The Committee simply does not see how such figures would be utilized in terms of the permit program.

f) **Some discussions at the meeting touched on the use of the benchmark dose as a means of dealing with non-cancer risks. The Committee would like to make some opinions known on this issue.**

There are several advantages of using the benchmark dose (Crump, 1984). The most important is that it allows use of all the available data to derive dose which can be used for developing an RfD. It derives a number that is largely independent of the spacing between doses and it can be utilized in such a way as to reflect the quality of the data that are available. The Committee generally endorses the use of the benchmark dose approach for these reasons, but emphasizing several potential pitfalls that should be avoided.

With the benchmark dose there is a tendency to utilize a low benchmark (e.g., an ED_{01} or even lower) to which uncertainty factors are applied to derive the RfD. Ordinarily the benchmark is taken to be the upper 95% of the point estimate made by the multistage model. The Committee urges the Agency to resist this temptation and select a point that is within the range that can be detected in toxicological studies that are currently in use (e.g., the ED_{10}), primarily because the confidence intervals of the estimate increase dramatically as the estimate decreases. The Agency is reminded that the basis of estimating risks from non-cancer effects assumes that there is some dose below which there is no effect. Application of uncertainty factors to the benchmark dose will

then drive estimated "safe levels" in any given media to very low levels, potentially lower than would be obtained if one were to assume that the LMS applied. Therefore, the Agency would find that low benchmark doses will be quite incompatible with MCLs derived by conventional means. However, if the benchmark approximates the response that is detectable in toxicological studies, the estimates should not vary significantly from those derived by conventional means.

3.4 Bioaccumulation Issues

The Drinking Water Committee cautions the Agency that the strategy of setting AWQC by measuring contaminant concentrations in certain biota and then applying either a bioconcentration factor (BCF) or a bioaccumulation factor (BAF) to calculate water concentrations may not accurately reflect the complex ways in which the real environment operates. This subject was extensively discussed in a 1993 SAB report which encouraged the Agency "*...to continue to explore these approaches*" (US EPA, 1993). However, this report also noted several potentially serious problems in the use of "field" BAFs, and it is worthwhile to quote at length from this document:

> *Field BAFs must be interpreted very carefully, and it should be recognized that they may contain substantial errors and variability due to the following reasons:*
>
> *a) Analytical methodologies generally determine total concentrations all of which may not be biologically available;*
>
> *b) There may be a loss of analyte by sorption or evaporation during sampling;*
>
> *c) Incomplete extractions may occur, especially if there is a high organic carbon content in the water;*
>
> *d) Temporal and spatial variability in water concentration may occur due to season, temperature, depth, hydrology, meteorology, and microbial and photolytic activity;*
>
> *e) There is likely to be variability in fish concentrations due to size, age, sex, season, pre- or post-spawning status, migration, the nature of and availability of food, the structure of the food chain, differences in lipid content, parasite infestation and general health of the organism.*

Given these potentials for error, EPA should discuss and quantify the variance in field derived BAFs in its guidance, along with FCM estimates, and attempt to identify the magnitudes of natural variability and analytical errors in each criterion data base, and estimate the impacts on the BCFs and FCMs.

In many cases, the laboratory-generated BCF data are likely to be more analytically accurate, but they may be less representative than BAF, in that they do not reflect natural variabilities, especially on food uptake. Therefore, field measured BAFs are suitable for the calculation of criteria ***but with the qualifications that the data must be interpreted carefully*** *and all information should be exploited. Specific guidelines need to be developed for the acceptability of residue data in tissues and dissolved concentrations in water. This will likely require a research effort to determine the appropriate sampling procedures, such as the number of organisms per station, the sampling frequency, or filtered/ unfiltered water.*

To help alleviate the problem, EPA needs to support a research program to develop more sensitive analytical methodologies for hydrophobic chemicals in tissues, sediments and water. Consideration should be given to the establishment of a formalized analytical chemistry program which utilizes the best scientists, the best instrumentation, adequate support, etc., to develop analytical methodologies and perform analyses that are not readily achievable by "normal" laboratories. Support to universities and industrial support to develop analytical reference materials would help ensure the success of the program.

The same document went on to caution the Agency that the techniques proposed "*...have not been applied to enough field conditions to judge if the predictions are realistic,*" and to note that they were "*...particularly concerned that metabolism is not included [in some of the theoretical modeling].*" Finally, the document concluded that this "*is clearly an area in which more research is needed.*"

The Drinking Water Committee is concerned that the Agency may have misinterpreted the above-cited SAB report as a blanket endorsement of these techniques for developing AWQC before a firm scientific basis for doing so has been developed. For example, we believe that the approximations proposed to estimate how much chemical is truly dissolved in water (i.e. available for uptake by the organism) based on organic carbon content, Log K_{ow}, and "total" content of the water need to be rigorously validated before they are used to establish AWQC.

As another example, studies which indicate a contaminant has a high octanol/water partition coefficient (K_{ow}) or BCF (measured when organisms are exposed to an artificially-maintained constant water concentration) *do not necessarily* indicate the contaminant will bioaccumulate in the environment. If the contaminant is subject to rapid hydrolysis, photodegradation, absorption, or metabolic transformation, the bioaccumulation potential will likely never be realized.

These criticisms should not be taken as a recommendation to relax standards or to ignore the potential for bioaccumulation where it is known to play an important role. However, it is the Committee's opinion that AWQC criteria must be based on sound environmental data and good science with a minimum number of assumptions. AWQC should not be driven by hypothetical assumptions that bioaccumulation *might* occur; they must be based on sound experimental evidence that bioaccumulation *does* occur. In general, the Committee feels that, for the time being, the Agency should focus attention on BCF rather than BAF, because of the higher likelihood of collecting an adequate BCF database. BCF can generally be measured in the laboratory with some confidence, while estimations of BAF involve incorporation of many as yet untested assumptions. Properly used, the BCF can provide a suitable basis for evaluating bioaccumulation potential.

3.5 Exposure Issues

3.5.1 Allocating the RfD

Before discussing procedures for allocating the RfD, the Committee would like to note that the RfD ordinarily describes a region of exposures which have been chosen to provide high confidence that human populations exposed to such doses will not develop adverse effects. Because of the conservative way in which RfDs are calculated, it is unlikely that exposure of any populations to doses slightly over the RfD (even up to twice the RfD) would produce significant health effects. Consequently the Committee does not feel that it is appropriate to develop AWQC geared to ensure that the sum of all theoretically possible exposures never exceeds the RfD by even a small amount.

a) **Should fish criteria be derived assuming that fish intake uses up all of the RfD?**

The question is ambiguous. We assume that the Agency means "Should fish intake and water consumption be combined in developing AWQC?" The answer to this question is that the Committee recommends developing separate criteria based on fish intake and water consumption (i.e., hypothetically using up all the RfD in each calculation).

For those few materials which strongly bioaccumulate in fish (BCF > 1,000) the human exposure from water consumption is negligible. For materials which do not bioaccumulate, the exposure from fish consumption is negligible. Therefore the Committee recommends developing separate criteria based on either fish intake or water consumption. Normally the most stringent of the two would determine the AWQC. Also, the calculation of two separate criteria might allow the flexibility of basing the AWQC on water intake rather than fish consumption in those cases where local populations are cautioned against eating large amounts of fish.

On the other hand, if the Agency means to ask "Should food, inhalation, dermal exposures, etc. be considered in setting the AWQC?," the answer is more complicated. The Committee recognizes that human exposures to substances present in fish may occur through other routes of exposure (i.e., in other foods or drinking water). However, we are concerned that if the Agency attempts to compensate for other routes of exposure (either by subtracting other inputs or by allocating only a certain percentage of the RfD for water exposures) they may focus intense regulatory attention on insignificant problems, thus wasting scarce resources that should be available for more significant health risks.

This is particularly true when reliable data regarding other possible routes of exposure are not available. In this case, the Agency should not use "defaults" or "high end estimates" of exposure. Use of defaults or high-end estimates may result in very conservative criteria being established for water without any real indication of risk.

Consequently the Committee recommends that unless reliable data are available which indicate that human populations actually encounter *total* exposures significantly in excess of the RfD, exposure from other routes should be neglected in calculations of AWQC.

b) **How should the RfD be allocated? Should the percentage, subtraction, or some other approach be used? Should a 20% floor and 80% ceiling**

be used? Should a default of 20% be used when there are inadequate data to quantify total background exposure? If not, how could anticipated sources of exposure be accounted for when data are inadequate to quantify total exposure?

The Committee feels that apportionment of exposure sources for development of AWQC can only be attempted *when reliable exposure data are available*. In the absence of such data, arbitrary "defaults" or "high end estimates of consumption" should not be used and the AWQC should be based on water sources only (as noted in 3.5.1a above). Even when reliable exposure data are available, the Committee feels that the "percentage" or "subtraction" methodology can easily result in the misallocation of critical resources to address insignificant risks. Instead of using either the "percentage" or "subtraction" methodology, the Committee recommends the approach outlined below.

If the exposure data indicate that *total* exposures are well below the RfD, there is no problem and the Agency's goal would be simply to develop criteria to ensure that a problem does not develop in the future. Adequately protective AWQC could then be developed by assuming that all of the RfD is available for the water route. By using this approach, human populations would only be exposed to levels slightly above the RfD, even in the unlikely event that water input increased to the level permitted by the standard, because the other routes contribute relatively small amounts to the TOTAL exposure.

Inherent in this recommendation is the assumption that exposure data will be periodically updated to ensure that *total* exposures do not increase significantly above the RfD due to sudden increases in other sources of exposure. On the other hand, if *total* exposures are at or higher than the RfD, then remedial actions may need to be considered. When exposure data indicate that each of several sources of exposure contribute significant fractions of the RfD (e.g., greater than 25%) then one is faced with a multi-media control problem. Even in these cases, however, it may not be reasonable to develop AWQC if "background sources" which are beyond human control are the major contributors to human exposures, particularly if the RfD has been derived with a substantial safety factor (e.g., cadmium, mercury, radon).

Furthermore, when multiple routes of human exposure exist the Agency needs to consider the relative cost effectiveness of control efforts in other media. If *total* human exposures can be reduced below levels of concern with two or more

alternate strategies, it makes sense to choose the least expensive approach. Consequently, this Committee endorses the recommendation from the AWQC workshop held by the Agency in 1992:

> "When significant contributions are expected from multiple sources, *[and the total of those contributions exceeds the RfD]* then bring into the discussion the offices or agencies responsible for addressing these other sources to allow for the development of an integrated management decision based on the relative source contributions and the ability to control exposures from the various sources. Include in these multimedia exposure discussions both noncarcinogenic and carcinogenic endpoints for the chemical of concern."

3.5.2 Exposure Route, Rate, and Duration Issues

a) Should there be separate criteria for drinking water and fish intake: a water column concentration to protect water consumers and a fish tissue concentration to protect fish consumers?

The Committee suggests that AWQC criteria for drinking water and fish intake be established independently (see 3.5.1a above). When the two criteria are not identical, then the lowest (most stringent) criterion should apply. If the two criteria are identical (would result in equal exposures), then the Agency might consider reducing AWQC by a factor of two.

b) Should the methodologies for developing MCLGs and AWQC for drinking water be consistent?

The Committee foresees considerable difficulty in using the concept of MCLGs in the development of AWQC. There are several reasons for this:

(1) The MCLG for carcinogens is arbitrarily set at zero. Introducing this concept into the AWQC is likely to confuse the public, distort the relative importance of carcinogens (versus untested contaminants), and result in the misdirection of resources if applied to the permitting process (e.g., PCBs, dioxins and dibenzofurans, trichloroethylene, tetrachloroethylene).

(2) The MCLG approach apparently underlies the Agency's decision to continue the practice of adding a safety factor for the presence of "weak" carcinogenic concerns (i.e., for certain Category C chemicals). This use of

the MCLG approach is not scientifically sound, however, because it incorrectly mixes two classes of effects; and there are sounder ways to achieve the desired end with such chemicals. For example, carcinogenic and non-carcinogenic effects might be considered separately, and the more stringent limit from appropriate estimates for each endpoint could be selected, or the two effects might be considered jointly, although this would involve a major departure from current practices.

(3) Concerns addressed in setting AWQC are considerably different from those applicable to drinking water rules. The differences include the possibility that AWQC will be based on bioaccumulation of chemicals in fish, the need to set criteria based on aquatic species, and the need to protect certain uses of the water (i.e., not setting an AWQC for a disinfectant by-product which subsequently precludes use of the disinfectant responsible for generating it in a downstream drinking water supply).

On the other hand, the derivation of the RfD (or potency factors for carcinogens) used to set the AWQC should be the same as the derivation of the RfD used to set the MCL. As data are updated in one program, they should be updated in the other. Nevertheless, determination of how these numbers are used to set AWQCs or MCLs involves risk management as well as risk assessment decisions. For these reasons the Committee considers that it may be reasonable to develop an AWQC different from a MCLG in certain specific cases.

c) **Should "one day" criteria using realistic single meal consumption rates be developed to address potential acute effects (including reproductive and developmental effects) from consuming contaminated fish?**

The Committee notes that current "average fish consumption" rates of 6.5 g/day may not be protective for potential acute effects associated with a large single meal. In the average American diet, we suspect that exposure is discontinuous, occurring at weekly or monthly intervals. We believe, therefore, that criteria for acute effects may need to be developed when it can be reasonably anticipated that single exposures may induce adverse effects in humans. The Committee cautions the Agency, however, to be certain that these criteria are not applied to adverse health effects which are not reasonably anticipated to result from single, acute exposures, and notes that public warnings may also be used to address special circumstances (e.g., pregnant women should avoid consuming large amounts of fish contaminated with developmental toxicants)

d) **Should there be separate criteria for incidental water intake from recreational use for situations where drinking water criteria are not used (estuaries) and fish ingestion or aquatic life criteria do not protect recreational users from incidental ingestion. For example, the existing fish ingestion criteria for phenol is 4,600 mg/L, while the one day drinking water health advisory is 6 mg/L. To prevent potential acute health risks from incidental recreational ingestion, an incidental intake rate (e.g., 0.01 L/day) could be used with acute toxicity data (e.g., one day drinking water health advisory value multiplied by 100?).**

The Committee feels it is unlikely that AWQC established to protect aquatic life in an estuary would permit contaminant concentrations high enough to represent an acute hazard to humans incidentally ingesting such a small quantity of water. In the example given (phenol) we feel it is improbable that 4,600 mg/L would not be deleterious to aquatic life and hence regulated on that basis. We feel that circumstances in which a separate criterion for incidental ingestion would be necessary are so rare that they do not warrant serious consideration by the Agency.

e) **Should water and fish intake assumptions be developed on a per kilogram body weight basis to use the actual body weights of survey respondents and to avoid the use of default body weight assumptions?**

In theory it would be better to develop standards on a per kilogram body weight basis. However, in practice the results are not different enough to make much difference in the magnitude of AWQCs. In particular, data should not be rejected because individual body weights are not available, and funds should not be allocated for collecting such data since no conceivable benefit would accrue.

3.5.3 Fish Consumption Rates

a) **Is it more defensible to include fish consumption in quality criteria with or without an assumed body weight? That is, should fish consumption rates be normalized to body weight or should we continue to assume an average body weight of 70 kg?**

This question appears to be a duplicate of Question 3.5.2e above, and the same answer applies.

b) **Is it technically defensible to use upper percentiles of national consumption surveys to represent special subpopulations such as recreational and subsistence fisherman ethnic groups?**

It is very difficult to account for the differing fish intakes of different populations through the development of AWQC focused on point source discharges. A central issue is that fish in a particular body of water are almost always impacted by a variety of sources. In many cases, the major sources are not subject to the permitting process (PCBs, Dioxins, Dibenzofurans). Consequently, it makes little sense to try to deal with recreational and subsistence fishermen on the basis of an AWQC.

The Committee feels that the best way to protect subpopulations with high fish consumption is to base health standards on the levels of chemical that are found in fish, not in effluents. Under such an approach, state and local authorities decide upon the safe levels of intake of particular chemicals and translate them into guidelines for the consumption of fish types that can be safely consumed from given bodies of water.

3.6 Microbiology Issues

a) **Would the establishment of a multi-organizational working group to provide recommendations to the EPA on technical considerations of this effort be appropriate to enhance progress on ambient water microbiological quality?**

The Committee believes that the establishment and implementation of such a working group with representation from EPA, The Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), academia, the water and wastewater industry, and the public would be highly beneficial. This is because the scientific and technical issues for the microbiological contaminants of human health concern go beyond the artificial jurisdictional boundaries of the regulatory and other federal agencies that deal with pollution sources, water pollution control, treatment of water and wastewater, fisheries resources and public health. Indeed, the development of such a multi-organizational working group would acknowledge this fact. Hopefully, such a working group would address microbiological contamination of ambient waters on the basis of the pollution types and sources, their transport through (and proliferation in) the environment, their partitioning among environmental compartments (e.g. water

column, sediments, fish), and their potential for human exposure via various water-related routes. Only by having expertise to deal with the science and technology of these phenomena, as well as the health effects and risks from such exposures, can microbiological contaminants in ambient waters be addressed in a rational and effective manner.

b) **Should ambient water quality criteria for microbes be developed for recreational, drinking sources, shellfish harvesting, reuse, irrigation, wetland and groundwaters? What should be the relative priority for establishing health criteria and monitoring requirements for these classes of water?**

There is clear justification and rationale for keeping recreational water quality criteria as a high priority. No other regulatory program or legislative mandate provides a clear basis for developing microbiological criteria for such waters, and adverse health effects have been documented by disease outbreaks and in epidemiologic studies. The Committee believes that despite the desirability of and need for a comprehensive and integrated approach to ambient water quality, it is unrealistic, perhaps inappropriate and in all likelihood impossible to address all of these water-related exposure routes of microbial health effects concern under this regulatory initiative. Historically, the ambient water quality criteria for microbes of human health concern have dealt primarily, if not exclusively, with recreational bathing waters.

In contrast to recreational waters, microbiological criteria for drinking source waters, ground waters and shellfish harvesting waters are or should be addressed through other regulatory programs, including the Safe Drinking Water Act (drinking source waters and ground waters) and the Food, Drug and Cosmetic Act (shellfish harvesting waters). Specifically, microbiological issues and criteria are being addressed through such drinking water regulatory initiatives as the Coliform Rule, the Surface Water Treatment Rule (SWTR), its revision as the Enhanced SWTR, the Ground Water Disinfection Rule, and the Disinfection By-products Rule. The microbiological quality of shellfish harvesting waters is addressed through the FDA's National Shellfish Sanitation Program and its agreements with the Interstate Shellfish Sanitation Conference, the EPA and the National Marine Fisheries Service. EPA is or should be a party to these agreements. What may be lacking are the communications and interactions between these various parties and their representatives in the scientific community. There should be coordination of activities among these programs and

agencies, and the establishment of a multi-agency working group, as proposed in A above, could greatly facilitate such interaction and coordination. This might help to prevent unwitting duplication of efforts, needless and wasteful competition for scarce resources, conflicting methodology for developing and implementing microbiological criteria, and unnecessary jurisdictional disputes.

The question of including AWQC efforts for reuse, irrigation and wetlands is not only difficult to address but also difficult to justify in the context of this regulatory effort. This is because human health effects from microbiological agents transmitted by these exposure routes are likely to be either negligible, too low to be documentable, or highly variable. For example, irrigation water quality criteria would be extremely difficult to establish because of the spectrum of potential quality requirements. Water used for irrigation may come from either ground or surface sources, may be subject to diverse and highly variable sources and amounts of human or animal fecal contamination, and may be subject to other quality criteria defined by the intended irrigation use. With respect to the last point, for example, microbiological criteria may differ for irrigation of fruits and vegetables to be eaten raw, fruits and vegetables that are cooked or processed before eating, non-food crops (fodder and horticulture plants), greenspace and forests. Because of the poorly documented, complex and apparently low exposures from these sources, the inclusion of irrigation water does not appear to be adequately justified at this time. There are analogous concerns about reuse and wetlands waters. Without better justification of potential exposure sources and transmission routes, the Committee recommends that these classes of water not be included in the effort.

c) **Should ambient water criteria for microbes be directed only at microbes causing gastrointestinal diseases or be expanded to cover other diseases?**

The Committee recommends that the process of developing and evaluating water quality criteria for microbes should include microbes causing fecally-transmitted diseases other than gastroenteritis, and also include microbes causing diseases of the skin, respiratory tract, eye, ear, nose, throat and perhaps other sites of entry and infection. The criteria development effort should also consider those animal pathogens that potentially infect humans, such as *Cryptosporidium* and *Giardia*. The reason for inclusion of these pathogens is that health effects from such pathogens, including illness from aquatic exposures, have already been documented in the scientific literature (Seyfried *et al.*, 1985; Sobsey *et al.*, 1993).

The Committee recommends that hazard identification for these other pathogens be included in the methodological process for development of the ambient water quality criteria.

d) Are the ambient recreational water quality criteria appropriate and transferrable to other high priority ambient waters?

The current ambient recreational water quality criteria are neither appropriate for nor transferrable to other ambient waters. The current criteria in the 1986 guidelines are based on densities of enterococci and *E. coli*, and the earlier criteria ("red book") are based on fecal coliforms. These indicator criteria were intended to address only those pathogens causing enteric (gastrointestinal) illness. They do not address the extra-enteral pathogens and their illnesses. Furthermore, the effectiveness or validity of these indicators to reliably predict health effects even of gastrointestinal illness has been questioned as misguided and has been challenged on the basis of contrary findings in epidemiologic studies of recreational water quality (Seyfried *et al.*, 1985; Cartwright, 1993).

e) Should the stringency for protection of public health be linked to the likelihood of human exposure to different types of ambient water?

The Committee recommends that the likelihood of human exposure to different types of ambient water be the basis for identifying the types of ambient waters for which criteria need to be developed, as discussed in d) above. The potential for human exposure and the risks of exposure are likely to differ greatly for the different ambient waters identified in f) below. The case for quality criteria for recreational waters has been established on the basis of documented exposures and health effects (illness). However, the case for exposures and illness from some of the other waters has not been established. Furthermore, some of the other ambient waters from which there are potential microbial exposures are and should be addressed through other regulatory programs, as noted in the response to b) above.

f) Is it appropriate to develop risk-based health criteria for pathogenic microorganisms in ambient waters?

The Committee believes that a risk-based approach to criteria for pathogenic microorganisms in ambient waters is both appropriate and feasible for at least some pathogens. This reflects the apparent consensus on this approach within the

scientific community (Sobsey *et al.*, 1993). Indeed, this approach has already been used for drinking water, has been attempted for sludge, and is being explored for shellfish and land-applied human excreta used in agriculture.

However, the Committee believes that there are limitations to the applicability of this approach to the quality criteria for microbial pathogens in ambient waters. Specifically, the Committee recommends that, initially, this approach can and should be directed only to those pathogens that are known to occur in and cause health effects from ambient recreational waters and for which dose-response and epidemiologic data are available. Examples are rotaviruses, adenoviruses and hepatitis A virus. The Committee believes, however, that there are major impediments to the implementation of this approach to the risk assessment of many pathogens, because of the lack of dose-response data and epidemiologic evidence of clear health risks from exposures via ambient waters.

g) Can strain or species differences in virulence be determined by monitoring?

The Committee believes that this question is difficult to answer in scientifically proven terms because of the lack of knowledge about virulence determinants, their expression by many of the potential waterborne pathogens, and their ability to be measured readily. The dearth of such data is important but not unique to the ambient water quality methodology initiative. Such data are also needed for other environmental routes of pathogen exposure, such as drinking water. For this reason, the Committee believes that further research has to be done on the identification, characterization and measurement of the virulence determinants of microbial pathogens and on the factors governing or influencing the expression of these determinants under different environmental conditions. Such information is needed before the question about monitoring for microbes on the basis of virulence can be answered effectively. Furthermore, the role of other factors in virulence expression, such as host factors, also must be addressed by research. The Committee recommends that this question be given a relatively low priority for ambient water quality criteria until the necessary research data are obtained.

h) How should EPA deal with injured organisms in risk assessment?

The Committee believes that this question identifies an important research need that goes beyond the scope of this initiative on the microbiological criteria

for ambient water quality. Presently, there are no microbial regulations for any waters that adequately consider the role of injured organisms. All of the current criteria and standards for microbes in water are based on concentrations of bacteria estimated by cultivation methods. Some efforts have been made to include "resuscitation" steps during cultivation (e.g., lower incubation temperatures for brief periods) and to use culture media that are less stressful or inhibitory to injured organisms. However, the health significance of injured pathogenic organisms remains uncertain. Some recent studies in the scientific literature indicate that injured organisms have dramatically reduced infectivity in terms of the dose of cells needed for infection and the potential to produce disease (as opposed to sub-clinical infection) (Jones *et al.*, 1991; Medema *et al.*, 1992). Hence, the public health significance of injured pathogens remains uncertain. For this reason, the Committee recommends that this issue is presently beyond the scope of this methodological initiative for ambient water quality criteria, and therefore is a low priority issue for this effort. Overall, it is a high priority question for the public health aspects of water microbiology, but the research needs go well beyond the domain of this initiative.

i) **Are current molecular techniques for pathogen detection/identification promising enough to push for their rapid development for routine water monitoring; can such techniques readily be made quantitative and capable of discriminating dead from viable organisms?**

The Committee believes that current molecular techniques for pathogen detection/identification in water and other environmental samples are still in their early stages of development, they lack adequate quantitation, and there is still the unresolved question of whether or not they can distinguish between live and dead (infectious versus non-infectious) organisms (Enriquez *et al.*, 1993; McCurty and Atlas, 1993). The research needs on these issues are substantial and as yet unmet. The Committee recommends that such research be done because of the enormous potential of these detection methods. However, as with some of the other issues raised in the workshop report and EPA's response, this issue is broadly relevant to microbes in a variety of waters and other environmental samples. Hence, it goes well beyond the scope of the ambient water quality initiative, and for this reason, the Committee recommends that it should be of low priority in the context of this regulatory effort.

j) **Are the currently approved indicator organisms and acceptable levels for them in beach waters appropriate for determining the safety of waters against gastrointestinal (GI) disease?**

The Committee believes that the currently approved indicator organisms in beach waters are probably appropriate for determining the safety of bathing waters against GI disease in at last some situations or settings. From the historical record of waterborne disease from bathing waters and the bacteriological quality of such waters, it is clear that fecal coliforms, *E. coli* and enterococci have the potential to indicate fecal and sewage contamination of bathing waters. Epidemiological studies at both marine and freshwater bathing beaches in North America have documented the effectiveness of these indicators in predicting risks of GI illness from bathing waters.

However, the Committee believes there are serious and justifiable concerns that the GI health risk data predicted by the existing indicators, and the standards for them can not be generalized to ALL bathing waters. Some of the reasons for this concern is the well-documented variability in the levels of indicator bacteria in sources of fecal contamination, the potential for some of these indicators to arise from non-fecal sources, and the variability in the quantitative relationships between these indicators and various GI pathogens in the sources of fecal contamination (Cartwright, 1993; Fleisher, 1991). For example, there is the variability in indicator bacteria densities and pathogen densities created by treatment and disinfection of sewage. In some situations treated effluents contain high levels of indicator bacteria because they are not disinfected and in other situations they contain low levels of indicator bacteria due to disinfection. Because of the comparative resistance of some of the important GI pathogens, such as enteric viruses and protozoan cysts, to wastewater treatment and disinfection, there is no consistent relationship between densities of these indicators and the densities of these GI pathogens. Hence, in some cases ambient bathing waters impacted by effluents will contain low indicator levels but relatively high levels of GI pathogens. The Committee believes that the currently accepted levels of the bacterial indicators are not uniformly and adequately protective of health risks from GI pathogens in bathing waters.

k) **Are the currently approved indicators predictive of other human diseases from fecal or other anthropogenic sources and from animal sources?**

The Committee believes that these indicators are not likely to be adequately predictive of the human health risks from non-GI illnesses associated with human or animal fecal contamination. Epidemiologic studies in other countries, including Canada and the United Kingdom, show that there are documented health risks from non-GI illnesses in bathing waters subject to fecal contamination, and that these risks are not reliably predicted by the fecal indicator bacteria now recommended by EPA (*E. coli* and enterococci) (Cartwright, 1993; Fleisher, 1991). The Committee recommends that in this initiative EPA consider the alternative and newer epidemiological data on bathing waters from such countries as Canada, the United Kingdom, Israel, South Africa, Hong Kong and other studies.

l) **Are there alternative indicator systems that warrant investigation for improving ambient water monitoring?**

The Committee believes there are candidate alternative indicators worthy of consideration and deserving of investigation in this initiative. The Committee believes that some of the examples mentioned in the workshop report and EPA's response are indeed worthy candidates for consideration. These include bacteriophages such as coliphages, *Clostridium perfringens* and rainfall events. The Committee recommends that EPA investigate the initiatives on bathing water quality indicators in other countries and geographic regions, such as that by the European Community.

m) **Is there a justification for developing different indicator organisms to monitor microbial pollution of tropical waters?**

Based on the limited studies now available, the Committee believes that the validity and usefulness of traditional or standard bacterial indicators of fecal contamination in tropical ambient waters is uncertain. While some studies indicate that coliforms, fecal coliforms and even *E. coli* and enterococci are ubiquitous in tropical ambient waters, the amount, quality and representativeness of these data are limited. The Committee believes that more and better studies are needed on the microbial ecology or natural history of these and other candidate indicator bacteria in tropical ambient waters. The Committee concludes that present information is too limited to draw firm conclusions about the usefulness and reliability of current indicators to monitor fecal contamination in tropical waters. The Committee recommends further investigation of this issue by EPA.

n) **Are there any significant issues related to ambient water microbial disease not covered by the Workshop report and EPA's response?**

The Committee believes that the situation is quite the contrary: there are too many issues and too broad an agenda raised by the Workshop report and EPA's response. The Committee recommends that EPA prioritize the issues and focus the agenda on the most crucial topics that are not covered by other regulations. The Committee recommends that EPA focus primarily on ambient recreational waters. These are the waters that have been historically addressed, there are clear exposure potentials and documented health effects, and furthermore, some of the other waters (drinking sources, shellfish harvesting and reuse) are covered by other regulations. For these reasons, the Committee recommends that efforts be made to integrate or coordinate the risk assessment for pathogenic microbes in ambient waters to the risk assessments being done for other waters, such as drinking water and shellfishing waters.

3.7 Minimum Data Requirement Issues

a) **Is the use of a tiered approach reasonable?**

The use of a tiered approach is reasonable. It must be made absolutely clear to the risk assessor and risk manager, however, that the categories are based on the *availability* of certain data elements, and that they do not reflect the *quality* of the underlying research. Obviously, the toxicity of the compound is also independent of the category.

b) **As presented, do the individual tiers reflect minimum requirements necessary for water quality criteria and interim effluent permit limit development.**

It is quite appropriate that Tier I should include mechanistic, pharmacokinetic and target organ toxicity data. The statement that for chemicals in Tier II there should be enough data to generate an RfD or cancer potency factor makes sense from the standpoint of having to have some breakpoint, but this concept is very poorly defined. The question is, if there was one reasonably good 90 day study which included a NOAEL dose level in one species, would a chemical qualify for Tier II?

Tier III presents some problems. The minimum of a 28-day study appears reasonable. The Committee agrees with the EPA that the purpose of this category is to generate some number for regulatory purposes while at the same time providing an impetus for additional research. The Committee is concerned with the possibility that whatever value was derived might *de facto* become permanent and strongly suggests that its temporary character be emphasized by the Agency. More and better data should be quickly rewarded. That is, the results of a complete and well conducted 90-day study might very well indicate that the chemical is not as great a concern as suggested by a 30-day study. In this case it would be appropriate for EPA to increase the value of the AWQC, on the basis of better data and less uncertainty. The question of what is done with group C carcinogens is difficult because it is not clear what the Agency means by "insufficient data." If a study were carried out long enough to convincingly demonstrate carcinogenicity in a laboratory animal species, it is difficult to imagine that there would be insufficient data either in that study or in other studies on that particular compound. The Committee recommends that EPA carefully evaluate whether or not this is a real problem. The Committee also recognizes that the new EPA Guidelines for Cancer Risk may be different and not have the C category.

Tier IV guidelines are also reasonable, as is the intention not to use these for standard setting. Obviously, if there are data that suggest potential hazards this information is important to communicate. Tier V guidelines are also reasonable.

c) **Under what specific circumstances should a Group C chemical be categorized under Tier III? Are there circumstances in which inadequately tested chemicals (currently categorized as Tier III) should be placed in Tier II in order to develop water quality criteria?**

There are two issues involved here. First, there is no apparent reason that group C compounds should be handled differently from those in other categories. For example, if there are good data on endpoints other than cancer, and perhaps even a good carcinogenicity study demonstrating positive results in one species, there is no reason why the chemical should be a Tier III. Alternatively, if the data base is poor, a Tier III categorization would be appropriate, although, as stated in part B above, the likelihood of this is open to some question.

The purpose of the tier system is to categorize compounds on the availability of information in their toxicity data bases, so that regulatory decisions can be made. It would be inappropriate, therefore, to move a chemical to a category where it does not belong so that a regulatory decision can be made. From the standpoint of public health, the Committee is of the opinion that allowing the states to use Tier III values to set permanent permit levels would be very risky.

d) **What specific requirements can be place on the use of 28-day study data in order to ensure the best quality data is used in developing Tier III interim toxcity values?**

This is a judgment call. Study design factors such as the number of animals used (and hence the ability to detect an effect), the number of dose groups and the spacing of the dose groups are certainly important. While two species may not be necessary, they are certainly a plus. To list a whole host of clinical pathology tests (cell counts, serum enzymes, electrolytes, glucose values, etc.) would be unwise. If one already knows the target organ, evaluation of parameters associated with the functioning of that organ can be much more important that a whole host of negative findings in other organs. Consistency of findings, both within a study and among studies, also has merit. There should be concern if a study does not establish a NOAEL although this might not be considered absolutely esential if there is a good dose response study such that a benchmark dose could still be established. In other words, the results of a well conducted study that does not establish a NOAEL, but which establishes a good dose-response relationship, utilizes adequate numbers of animals, etc., may be of higher quality and engender greater confidence in the resulting estimates than the results of a poorly conducted study which "finds" a NOAEL primarily because it wasn't truly adequate in these same parameters.

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